REMARKS/ARGUMENT

Claim 15 has been amended to delete the reference to "infusion" and it is respectfully submitted that as a result, the objection to claims 16 and 17 as being in improper dependent form has been rendered moot.

The independent claims in this case, claims 1 and 15, have been amended to indicate that the active materials in each of the pair of pharmaceutical compositions have been kept separate. Thus, the composition which contains the α-ketoglutarate and/or α-ketoglutaric acid does not contain the ammonium and the composition which contains the ammonium does not contain the α-ketoglutarate and/or α-ketoglutaric acid. See, e.g., page 10 of the present application. As a result of this clarification, it is respectfully submitted that the prior art rejection should be withdrawn.

The claims were rejected under 35 USC 103 over Veech in combination with Vinnars. This rejection is respectfully traversed.

Veech teaches a parenteral nutritional solution which comprises water having dissolved therein at least one of the metabolizable nitrogen containing compounds set forth in Table 5, at least one carboxylic metabolite anion selected from a group of materials which includes α-ketoglutarate and at least one cation selected from a group which includes ammonium. These nutritional solutions reflect the (incomplete) composition of human plasma given in Table 3. The reference teaches at column 14, lines 18-20 that the presence of "alphaketoglutarate and NH_4^+ in an amino acid solution containing glutamate can control the redox state of the mitochondria." The next paragraph indicates that one can avoid the use of free ammonium. However, there is no teaching or suggestion of separating the alphaketoglutarate and ammonium in separate compositions for any reason, much less for concomitant administration. Whenever both alphaketoglutarate and an ammonium material are present, they are always both in the same composition. There is nothing in this reference which would motivate one skilled in the art to separate them into individual compositions.

The Vinnars patent teaches the addition of α-ketoglutarate, alone or in combination with conventional amino acid solutions, to a parenteral nutrition program. No reference to the use of an ammonium material in this reference has been found. Accordingly, this reference does not

teach or suggest keeping the α-ketoglutarate or α-ketoglutaric acid in a separate composition from ammonium.

The present invention provides a specific dosage unit comprising two separate compositions, one containing α-ketoglutarate and/or α-ketoglutaric acid and the other containing ammonium. The provision of these agents and separate pharmaceutical compositions is called for by the specific manner of their administration as disclosed in the specification and in the method of treatment claims. The efficacy of the method of the present invention and the unobvious superior usefulness of the combination of the compositions of the invention is not disclosed or suggested by the Veech or Vinnar patents, whether considered alone or in combination.

For the information of the Examiner, there is submitted herewith a copy of an editorial opinion as well as an article by Wirén et al. which questioned the rationale for providing an α-ketoglutarate rich diet to post-operative patients. These reflect on the continued validity of the broader aspects of the references upon which the Examiner has relied but still fail to recognize that the separating of the α-ketoglutarate and ammonium into individual compositions provides a superior usefulness as demonstrated in the present application.

In light of the foregoing considerations, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully solicited.

Respectfully submitted,

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APPENDIX A
Version With Markings To Show Changes Made
37 C.F.R. § 1.121(b)(1)(iii) AND (c)(1)(ii)

CLAIMS:

1. A method of preserving bodily protein stores in a catabolic patient, comprising the concomitant administration of a pair of pharmaceutical agents consisting essentially of (a) a first composition containing at least one of α-ketoglutarate and α-ketoglutaric acid and being devoid of ammonium, and (b) a second composition containing ammonium and being devoid of a α-ketoglutarate and α-ketoglutaric acid, the amounts of the pair being effective to preserve skeletal muscle.

15. A pharmaceutical dosage unit comprising a first pharmaceutical composition comprising at least one of α-ketoglutarate and α-ketoglutaric acid in a pharmaceutically acceptable carrier and being devoid of ammonium, and a second pharmaceutical composition comprising ammonium in a pharmaceutically acceptable carrier and being devoid of α-ketoglutarate and α-ketoglutaric acid, the total amount of the at least one of α-ketoglutarate and α-ketoglutaric acid and the ammonium being effective to preserve skeletal muscle, and wherein the amount [of infusion] administrated of said at least one of α-ketoglutarate and α-ketoglutaric acid is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ and the amount of infusion administrated of NH_4^+ is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 20 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.